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Literature Review

# Prevalence of Deep Vein Thrombosis among Patients Admitted for Non-Traumatic Swelling Lower Limb at the Adult University Teaching Hospital, Lusaka, Zambia

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## Abstract

Deep vein thrombosis (DVT) is a great concern worldwide in patients with non-traumatic swelling limb since it may be complicated with fatal pulmonary embolism (PE). The objective of this study was to explore the prevalence of DVT among patients admitted at the Lusaka Adult Hospital with non-traumatic swelling lower limb and possible associated demographic and clinical risk factors. A cross sectional analytical study was conducted on an 83-adult-patient sample admitted using a prepared questionnaire to record patients' socio-demographic characteristics, medical history data, physical examination signs and results from laboratory test and compressive ultrasound scans of recruited patients lower limbs. The chi-square, Kruskal-Wallis and t-tests served respectively to compare and assess associated variables of interest.

In this series of the patients admitted with swelling lower limb, the prevalence of DVT was 13, 3% (11/83) of which 6% located distally (popliteal veins) and 7, 30% proximally (iliac vein: 4% and femoral vein: 5,5%). The predominant age group ranged between 26 - 45 years. The association of physical signs and DVD was significant: ($p < 0,01$) mainly unilateral swelling (8/11), local warmth and tenderness (6/11) as well as the presence of varicose vein and the history of diabetes mellitus; in contrast to age, gender and drugs habits and tobacco.

The conclusion of the study is that the prevalence of DVT is high among patients presenting with non-traumatic swelling lower limb. Apart from varicose veins (sometime sign of possible obstruction of the deep vein blood retour), all patients discovered with DVT had well known clinical inflammatory signs and could have taken benefits of thrombo-embolism measures and could, then, safely and if necessary, undergo further explorations for other venous causes (primary venous insufficiency), arterial conditions (aneurysms, atherosclerosis) and lymphatic diseases. However, a more prospective and analytic study is recommended for more data and wider sample size.

***Keywords:*** *Deep Vein Thrombosis; Venous Thrombo-Embolism; Swelling Limb; Compressive Limb Ultrasound Scans*

## Background

Despite its occurrence in some ambulant individuals, mainly under specific medications like antibiotics, hormones, chemotherapy, antidiabetic, and psychiatric drugs, a thrombus is usually formed in hospitalized patients' vein in which Virchow's syndrome conditions are fulfilled (venous micro trauma by increased platelets secondary to stasis). A deep vein thrombus, an aggregation of blood platelets (thrombocytes) then causes an intravenous hydrostatic dysfunction of returning fluid above and around the obstacle that increases intravascular pressure leading to fluid extravasation to interstitial tissue (oedema). At the level of limb, mainly lower limb, a DVTT is then the leading cause of limb oedema or swelling limb.

The clinical concern about a DVT is the fact that it is first free in the venous lumen (phlebothrombosis) before it involves the venous wall and adheres to it (thrombophlebitis). During the phlebothrombosis period, a piece of the thrombus, embolus, may detach from it and migrate (thrombo-embolism). The thrombo-embolism is of a tremendous clinical concern since its morbidity and mortality are high worldwide. The embolus may end to block blood supply to vital organs like lungs causing pulmonary embolism (PE) even in a stable patient who suddenly changes condition. The embolus may also end in the heart, the brain or any part of the body where it may cause ischaemic injury, tissue damage and organ death. The commonest clinical presentation of DVT is swollen lower limb [1] to which may be added other signs from physical examination. Laboratory tests exist but nonspecific. Affordable imaging is provided by ultra-sonographic scan. Other non-invasive imaging is provided by Computerized Tomography and Magnetic Resonance but not cost effective. The venography m is specific but quasi invasive [2].

Swollen lower limb conditions are common surgical consultations attended to by surgeons. They have been classified by Godman., *et al*. 2001. The two predominant are venous (DVT) and lymphatic (lymphoedema). They remain a life threatening condition that may lead to death or to high mortality [3]. Many factors influence the outcome. In Zambia, the mortality rate of lower limb surgical disease ranked 6$^{th}$ in first quarter, 2019 among common causes of mortality at the UTH Department of surgery in the form of gangrene alone. The cause of death sudden in most cases is attributed to sepsis (a diagnosis of exclusion with a slow progression) and the possibly direct, manageable cause (thromboembolism) still under investigation (Surgical Audit, 2019).

### Statement of the problem

As highlighted in UTH Surgical audit, 2019, the mortality rate from non-traumatic swollen lower limb conditions at this institution is very significant representing 30% (9/96). Moreover, among the 9 deaths under swollen limb, 7 were sudden and one suspicious of PE suggestive of thromboembolic phenomena. But the relationship is not made as complication of DVT as reviewed in literature.

As noted by Wendelboe., *et al*. [4], public awareness is substantially lower for PE (54%) and DVT (44%) than for heart attack (88%), and stroke (85%). Hence a number of these mortalities could be reduced if patients with spontaneous swollen lower limb are screened for DVT at presentation and positive measures taken while still investigating for other causes.

### Justification of the study

Surgical Audits at the UTH have shown that among non-traumatic swollen lower limb patients who (30%) die, 28% had unexplained/ sudden deaths which could be attributed to thromboembolic phenomena as complication of DVT as reviewed in literature.

Still the prevalence of DVT is not known for this category of patients at their presentation at the institution. Hence the need to identify this gap (prevalence) and factors associated. This will allow early positive measures against the thromboembolism while still investigat-

ing for other causes of non-traumatic swollen lower limb.

These information will bring change on to manage for the DVT, swollen lower limb in terms of police making, relevant statistics an d optimal treatment to ultimately decrease morbidly and mortality related to lower limb swelling.

## Study Question and Objectives

What is the prevalence of DVT among patients admitted with non-traumatic swollen lower limb at the Adult University Teaching Hospital, Lusaka, Zambia? The main objective was to evaluate the prevalence of DVT among the patients admitted for non-traumatic swollen lower limb at this setting. As specific objectives the study had to determine the frequency of patients admitted with non-traumatic swollen lower limb; to determine among them the proportion of patients with DVT; to establish the demographic and clinical characteristics of patients with non-traumatic swollen limb and to establish relationship between DVT and sociodemographic and clinical factors.

## Literature Review

Globally the prevalence of DVT in patients presenting with lower limb swelling is variable. Cases of lower limb swelling with DVT are to a large extent clinically occult and thus a high index of suspicion is warranted. The known risk factors or variable may not be predictive of DVT.

The studies done on the American continent show significant but variable prevalence of DVT in patients with superficial phlebothrombosis (ST) T or cellulitis with swelling of the lower limb as the clinical presentation variable. In an USA prospective study performed by Skillman., *et al*. in 1989; A follow up (prospective) study of 60 cases in Brazil, by Sobreira., *et al*. in 2009 [5] on the prevalence of DVT and PE in ST, revealed that in 13 ST cases (21.67%) there was concomitant DVT and 17 ST patients (28.33%) also had PE. 11 patients had a clinical status suggestive of DVT, but only in 8 of these (61.5%), this clinical diagnosis was confirmed. None of the variables studied was predictive of DVT or PE. In Canada, Mortazavi., *et al*. in 2013 [6], conducted a study on the incidence of DVT in erysipelas or cellulitis of the lower extremities.

In Australia, a prospective study to determine the incidence of DVT in patients with ST in 1993 by Jorgensen., *et al*. using a Duplex Ultrasound a cohort of 44 patients admitted to a vascular unit. 10 of the 44 patients (23%) and proximal-vein thrombosis was found in 4 (9%). Four of these were not in continuity with the superficial thrombus. Maze., *et al*. 2013 in New Zealand went further to do a prevalence study of concurrent DVT in patients with lower limb cellulitis: a prospective cohort study. 200 patients assessed for DVT. 20% of subjects were high risk by Wells criteria. D-dimer was elevated in 74% and 79% underwent intonation of the affected leg. Ipsilateral DVT was found in 1 patient (0.5%) and non-ipsilateral VTE in a further 2 (1%).

Studies done in Europe conclude a variable prevalence: Dewar., *et al*. [7] in the UK and Geersing., *et al*. [8] in Netherlands.

In Africa, results look to be higher but variables: Bersier., *et al*. (2003) in Switzerland and Mangeni., *et al*. (2006) in Uganda. Around Zambia, some studies have been published as mentioned above in Uganda. No Local studies have been published on the association of lower limb swelling and the occurrence of DVT. However, similar studies in different study populations are comparable. In Zambia Chibeza., *et al*. [2] have written on the prevalence of DVT in patients with pelvic, femoral and tibia/fibular fractures at the UTH: 10.8%. In 2016, Mwandama., *et al*. [9] followed up on DVT and associated factors in adult medical patients admitted to the UTH (the prevalence of 11.1%) and in 2018, West., *et al*. [10] on prevalence of acute DVT according to HIV status following major orthopaedic surgery (prevalence was 4.8%). Furthermore, Odimba., *et al*. did two (2) studies on lower limb disease associated with swelling. The first being a study on "Improved outcome in fat embolism syndrome following ipsilateral femoral and tibial fractures" [11]. The second being, good outcome with surgical sympathectomy in critical limb ischaemia at the UTH [12].

### Methodology

The study employed a cross sectional analytical study conducted in the Department of Surgery at the University Teaching Hospitals, Lusaka, Zambia over 12 months, from June, 2020 to May, 2021. It targeted all patients admitted with non-traumatic swollen lower limb as a major cause of admission or reason.

The sample size was calculated using de prevalence formula with an estimated prevalence of DVT of 6% of similar work built half done by Mwandama., *et al*. [9] and with 0,05 confidence. It gave a sample of 86 which was then standardized for a finite population of 2500 (total number of patients admitted over a 6-month period in the surgical admission ward) and the sample was 83. The sample included all adults (18 years and above) admitted with non-traumatic swollen lower limb who consented to participate in the study excluding only those patients already known as having DVT. The sampling was a probability technique one for all non-traumatic swollen lower limb patients by randomization from admission ward and following a pre-established questionnaire of variables which focused on patients' social demographic data, medical history for risk factors for DVT, physical signs suggestive of DVT or alternative diagnosis and results from laboratory investigations and compression USS for both lower limbs and lower limb x-rays done within 24hrs. The dependable variable was the DVT/NO DVT. All data entered in an Excel spread sheet and exported to SPSS version 25 for analysis. Continuous data was analyzed using means and standard deviation if normally distributed and compared by t-test. If not normally distributed, median and interquartile range were used and compared by Kruskal-Wallis test. Categorical data were reported as proportions (frequencies and percentages) and tested for significance using Chi-square and fisher's exact test where applicable.

All ethical considerations were observed: safety, confidentiality, explanation, consent form, administrative authorizations. Ethical clearance and approval was obtained by the Zambia biomedical research ethics committee (UNZABREC).

Among the study limitations must be noted. The characteristics of the sample, its size despite being calculated with a fair formula and the restricted tools especially on laboratory ground without neglecting the pandemic atmosphere within what the study was undertaken

## Results and Discussions

### Determination of the number of patients admitted with non-traumatic swollen lower limb

As shown in figure 1 (Pie chart 1) of the 336 patients admitted to the surgical wards over the study period, 83 were enrolled into the study as non-traumatic lower limb swelling. This gives an incidence of 14% during the period of spontaneous lower limb swelling conditions among other admissions in General Surgical Units at the Institution. As it is the first study at the institution discussing this condition and for one year duration, the percentage of the condition constitutes at the same time the prevalence of non-traumatic conditions.

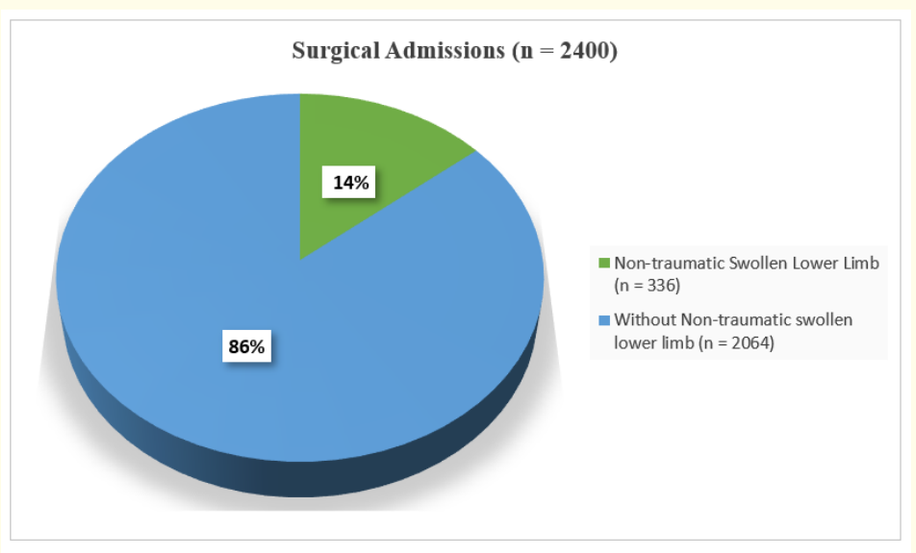


***Figure 1:*** *Impact of non-traumatic swelling limb during the study period.*

The study thus shows that this condition is a real component of the surgical burden disease in the department. Almost 15 patients out 100 admitted in general surgical units are for "swelling lower limb". The reviewed literature did not come across about the prevalence or the incidence of non-traumatic lower limb swelling in General surgical wards. The samples noted during this literature review reveal specific types of lower limb swelling as: superficial thrombophlebitis (Skillman., *et al*. in 1989 [13], and in Brazil, study Sobreira., *et al*. in 2009 [5]), cellulitis of lower limb or erysipelas [6], traumatic situation (Chibeza., *et al*. [2] and 2018, West., *et al*. in 2018 [10]).

## Determination of the prevalence of DVT in the now-traumatic lower limb swelling

The prevalence of DVT in this study population was 13.3 % (11/83) as illustrated in the pie chart or figure 2.

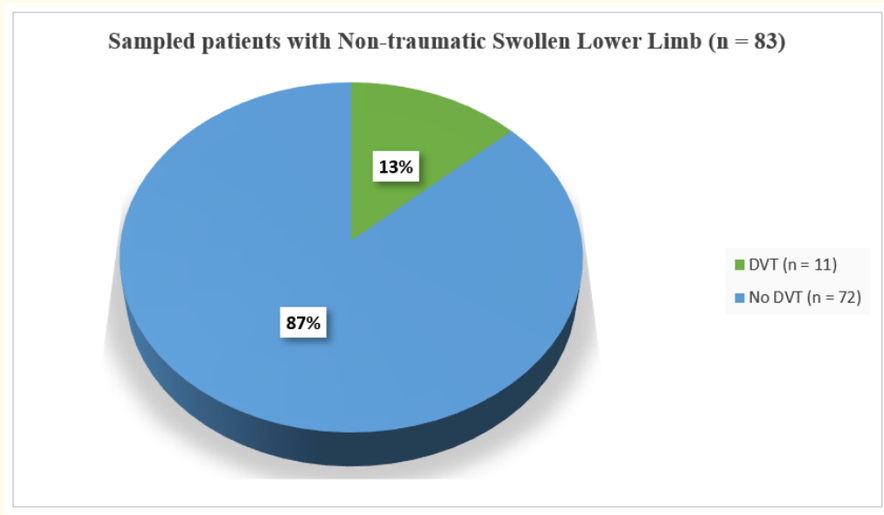


***Figure 2:*** *Prevalence of DVT of the study.*

The anatomical level on the veins with DVT is indicated on figure 3: 4/11: iliac vein (36,4%), 2/11 femoral vein (18,2%) and 5/11 popliteal veins (45,4%). With regard to recruited patients the prevalence of popliteal lower limb DVT was 6% in this study compared to the prevalence of iliac vein DVT (4.8%) and femoral vein DVT (2.4%). In this series, DVT are relatively high and could easily migrate through the inferior vena caval.

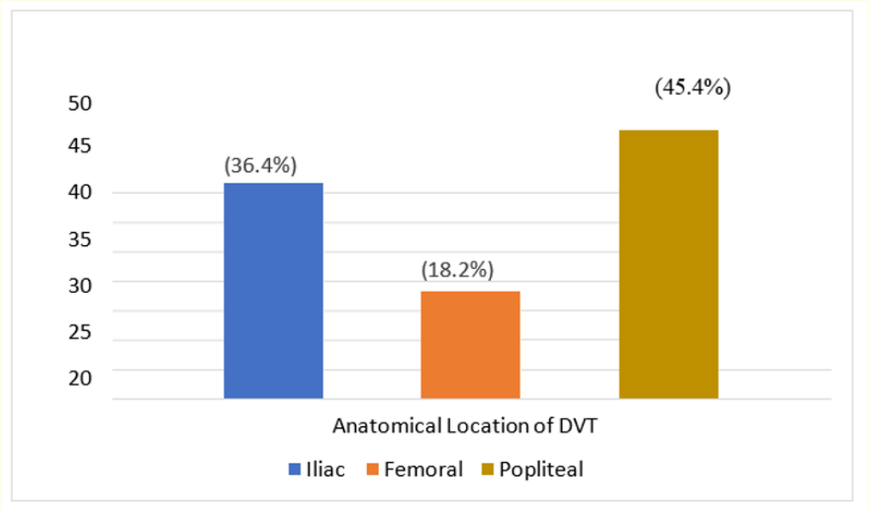


***Figure 3:*** *Anatomical distribution of lower limb DVT by bar graph.*

Comparatively to that from literature, this DVT prevalence is significantly high but, as it was priory said, the variability relays on clinical circumstances. The findings are similar to those from ARTEMIS and PREVENT studies reporting DVT prevalence range from 4.96 to 14.9% and indicating anatomical prevalence lower/proximal DVT of 3.4% and 5% respectively (Cohen., *et al*. 2006; Leizorovicz., *et al*. 2004). These findings however are different from Mwandama., *et al*. [9] who found a DVT prevalence of 11.1% and higher proximal lower limb DVT of 9.1%.

The side of the DVT and the swelling limb. In this study, eight patients had unilateral swelling and three had bilateral swelling from those with DVT. Even if the two iliac thrombi blocked the portal cave vein junction, the third bilateral edema cannot be explained by the thrombi. It could be explained by other cause of swelling limb. So, all the swelling limb was not secondary to DVT.

### Determination of sociodemographic and clinical characteristics, Risk factors)

### Sociodemographic factors and impact

The results of these factors are analyzed on table 1 with age, gender and smoking were analyzed in this study as demographic factors.

| Characteristics | Presence of DVT | | p-value |
|---|---|---|---|
| | Yes (%) | No (%) | |
| **Age group (years)** | | | 0.849 |
| 18 - 25 | 3 (15) | 17 (85) | |
| 26 - 45 | 4 (13.3) | 26 (83.7) | |
| 46 - 64 | 1 (6.7) | 14 (93.3) | |
| ≥ 65 | 3 (16.7) | 15 (83.3) | |
| **Gender** | | | 0.843 |
| Male | 7 (12.7) | 48 (87.3) | |
| Female | 4 (14.3) | 24 (85.7) | |
| **History of Smoking** | | 0.395 | |
| Yes | 3 (20) | 12 (80) | |
| No | 8 (11.8) | 60 (88.2) | |

***Table 1:*** *Demographic characteristics.*

With regard to age, in this study the youngest was 18 years old and the eldest more than 65 years old. The predominant group of ages was between 26 - 45 years. Patients with DVT in this study were relatively younger compared to those in other studies. In the Prevent study, minimum recruitment age was 40 years (Leizorovicz., *et al*. 2004). In the Artemis, 60 years was the minimum age of recruitment (Cohen., *et al*. 2006). In Mwandama., *et al*.'s [9] study, the patients were aged 40 years or more. Among the patients with DVT, 72.7% (8/11) were 26 years or older in this study. However as noted on table 1, the seeking of significant difference between the age-groups has not shown any substantial statically difference

It is the same for the gender and the smoking habits. There were more males than females and there were in the sample more no smokers than smokers, but as it is illustrated in table 1 there was no significant of the occurrence of DVT neither the gender nor the tobacco consumption. This corroborates read literature where such relation was not mentioned.

### Analysis of patients' medical history and the occurrence of DVT in non-traumatic swelling lower limb

The analysis results are provided on table 2 about the targeted conditions: HIV/AIDS, bedridden duration, duration of swollen limb, Family history of DVT, diabetes mellitus, previous major surgery, previous puerperium, and consumption of various medication (hormones, oral contraception drugs); When trying to find out the significance of the variable with the occurrence of the DVT by the use of the, p value , some circumstances are more closer than others like it is shown on the table 2: Not a single reveals statistically significant at 0,05. There are some interesting p. values like for the history of Diabetes mellitus (0,09), Number of days of bedridden (0.132), Recent Major Surgery (0.160), Duration of lower limb swelling (0.190) and HIV status (0.242). Hence variability among literature findings. In

| | Presence of DVT | | |
|---|---|---|---|
| **Characteristics** | **Yes %** | **No %** | **p value** |
| HIV positive status | 1 (5.3) | 18 (94.7) | 0.242 |
| Patients on ART | 1 (5.9) | 16 (94.1) | 0.315 |
| HIV Reactive patients | | | 0.502 |
| **CD 4 count** | | | |
| Absolute | 2 (10.55) | 17 (89.5) | |
| Unknown | 8 (14) | 49 (86) | |
| Duration of lower limb swelling | 2.7 ± 0.65 | 2.5 ± 0.63 | 0.190 |
| Number of days bedridden | 2.6 ± 0.55 | 3.2 ± 0.83 | 0.132 |
| Recent bedridden | 5 (17.2) | 24 (82.8) | 0.432 |
| Family history of DVT | 5 (14.3) | 30 (85.7) | 0.813 |
| Oral contraceptive use | 3 (17.6) | 4 (82.4) | 0.474 |
| Puerperium | 5 (15.8) | 16 (84.2) | 0.741 |
| Recent Major Surgery | 3 (7.7) | 36 (92.3) | 0.160 |
| Diabetes mellitus | (23.8) | 16 (76.2) | 0,099 |
| Primary diagnosis | | | 0.980 |
| Gangrene | 2 (14.3) | 12 (85.7) | |
| Lymphoedema | 2 (10) | 18 (90) | |
| Diabetic foot | 0 | 1 (100) | |
| Active malignancy | 1 (14.3) | 6 (85.7) | |
| Varicose vein | 6 (14.6) | 35 (85.4) | |

***Table 2:*** *Characteristics of medical history's significance (p value).*

Mwandama., *et al*. [9] study showed that 58% of the patients were HIV positive with 43.2% on ART. This study showed that of all HIV positive patients, only one patient had DVT while in Mwandama., *et al*. [9] 70% of patients with DVT were HIV positive. The variability is also in the primary diagnosis as it is shown on the table 2, the overall significance is only at p 0.980.

**The table 3 analyzes the findings from physical and laboratory examination:** Distribution of the swelling; DVT Inflammatory signs, BMI, pitting edema, varicose collateral superficial vein, full blood count, haemoglobin, white cell count platelet count, blood sugar control. The majority of patients were overweight with a mean BMI of 25.5 (SD = 2.34). Concerning the local physical signs and DVT, it was observed the following: exaggerated entire limb swelling, in three patients while eight patients had only leg swelling; Pitting oedema was observed in three patients witnessing high hydrostatic pressure; Five patients with DVT had local tenderness along the distribution of deep venous system; Five patients had varicose collateral superficial veins; Six patients had classical inflammatory signs of DVT with warm to touch on swollen limbs and Hoffman's positivity.

| | Presence of DVT | | |
|---|---|---|---|
| **Characteristics** | **Yes (%)** | **No (%)** | **p-Value** |
| **Physical** | | | |
| Body Mass Index | 25.6 ± 2.11 | 25.5 ± 2.38 | 0.927 |
| Type of swelling | | | < 0.01 |
| Bilateral | 3 (13) | 20 (87) | |
| Unilateral | 8 (13) | 52 (87) | |
| Entire Limb swelling | 2 (16) | 10 (84) | 0.01 |
| Leg Swelling Only | 9 (13) | 62 (87) | < 0.01 |
| Pitting Oedema | 1 (100) | 0 | 0.01 |
| Localized tenderness along deep venous system | 5 (100) | 0 | < 0.001 |
| Varicose Collateral superficial veins | 4 (80) | 1 (20) | < 0.001 |
| Warmth to touch | 6 (100) | 0 | < 0.001 |
| **Laboratory findings** | | | |
| **Blood glucose control n %** | | | |
| Controlled | | 16 | 76.2 |
| Uncontrolled | | 5 | 23.8 |
| Haemoglobin count (g/dL) (M ± SD) | | 10.45 ± 1.75 | |
| Platelet count (*109/l) (M ± SD) | | 261.2 ± 67.64 | |
| White cell count (*109/l) (M ± SD) | | 5.95 ± 1.20 | |

***Table 3:*** *Physical, laboratory, ultrasonography characteristics signs and significance with DVT.*

But as it might be noted from table 3, the contributing signs to the association between swelling lower limb and DVT are those having a p value significant: like unilateral swelling, inflammatory including local warmth and tenderness, pitting edema. Varicose vein may sign an obstruction of deep vein circulation but appear late. For diagnosis purpose the ultrasound scan is non-invasive and cost effective.

The Doppler ultrasound scanning confirmed 7 DVT on left lower limb, and 4 on right lower limb indicating apparent predominance of left side in this series [14-17].

## Conclusion/Recommendation

This study undertaken on a randomized sample of 83-patient admitted for non-traumatic swelling lower limb in the department of surgery revealed a high prevalence of 13,3% of deep vein thrombosis. 6 patients developed thrombus at high level (four 2 iliac and 4 femoral thrombi) with high risk of embolization; and 5 in popliteal vein. There was non-reported cases of diagnosed thrombo-embolism but cases of sudden death were noted. The number of patients admitted with non-traumatic swollen lower limb at the UTH was significant, 14% of the total admissions during the study period.

The predominant associated sociodemographic and clinical factors were the following: Predominant age-group between 26 - 45 years; More males than females; Clinical history of HIV/Aids on ART or not, diabetes mellitus; medications consumptions; anaemia and other laboratory signs (Full blood count, haemoglobin, white cell count platelet count, blood sugar control); physical signs of leg inflammation. However, in general, there was no statically difference between the occurrence of DVT and the social demographic and clinical characteristics when trying to ascertain the p value with regard to ages, gender, drugs or tobacco consumption; despite some circumstances being

more closer than others like diabetes mellitus (pv: 0,09), some HIV status (pv: 0242), duration of the swelling limb (pv: 190), duration of bedridden, history of major surgery (pv: 0160) or the family history of DVT (Inflammatory signs, pitting edema, varicose collateral superficial vein, BMI of 25.5 (SD = 2.34). The same, the findings from the distribution of the swelling could not be related exactly to the DVT: exaggerated entire limb swelling (in three patients) while eight patients had only leg swelling; Pitting edema was observed in three patients witnessing high hydrostatic pressure; Five patients with DVT had local tenderness along the distribution of deep venous system; Five patients had varicose collateral superficial veins; Six patients had classical inflammatory signs of DVT with warm to touch on swollen limbs and Hoffman's positivity. Only have significant value: unilateral swelling, inflammatory including local warmth and tenderness and pitting edema. Varicose vein may sign an obstruction of deep vein circulation but appear late. For diagnosis purpose the ultrasound scan is non-invasive and cost effective value. These clinical findings should be enough to recommend the thrombo-embolism prevention when continuing to seek alternative causes of non-traumatic limb swelling.

However, a wider and cohort prospective study is recommended to increase the sample size with more pathogenetic and aetiological components to study deeply this challenging general surgery of spontaneous swelling limb.

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